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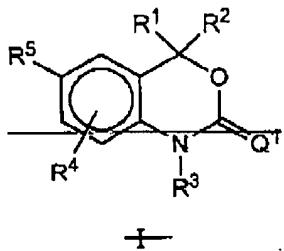
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AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1 (Currently Amended). A method of inducing contraception comprising the step of delivering to a female of child-bearing age a composition comprising a compound of formula I or formula II, or a tautomer thereof, in a regimen which involves delivering a pharmaceutically effective amount of one or more of a selective estrogen receptor modulator to said female, wherein formula I or II is:



wherein:

~~R¹ and R² are independent substituents selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₂ to C₆ alkenyl, C₃ to C₈ cycloalkyl, phenyl, and thiophene;~~

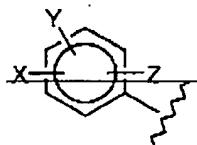
~~or R¹ and R² are fused to form a carbon-based 3 to 8 membered saturated spirocyclic ring;~~

~~R³ is H;~~

~~R⁴ is H;~~

~~R⁵ is selected from the group consisting of (i) and (ii):~~

~~(i) a substituted benzene ring having the structure:~~



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~~X is selected from the group consisting of halogen, CN, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, C₁ to C₄ alkoxy, NO₂, and C₁ to C₃ perfluoroalkyl;~~

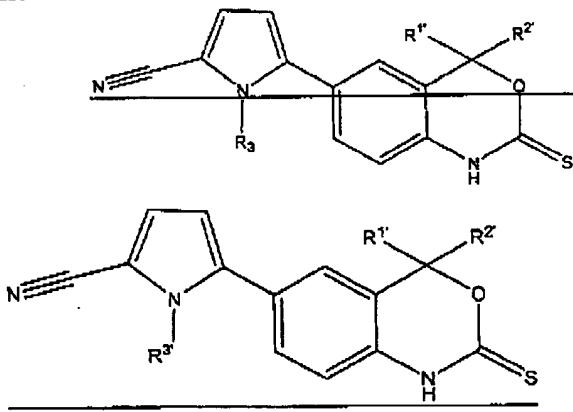
~~Y and Z are independent substituents selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₄ alkoxy, C₁ to C₄ alkyl, and substituted C₁ to C₄ alkyl; and~~

~~(ii) a five or six membered carbon based heterocyclic ring having in its backbone 1 heteroatom selected from the group consisting of O, S, and NR⁶ and having one or two independent substituents selected from the group consisting of H, halogen, CN, C₁ to C₄ alkyl, and substituted C₁ to C₄ alkyl;~~

~~R⁶ is selected from the group consisting of H, C₁ to C₄ alkyl, and C₁ to C₄ CO₂alkyl;~~

~~Q⁺ is S;~~

and formula II is:



II

wherein:

R^{1'} is selected from the group consisting of methyl, ethyl, and trifluoromethyl;

R^{2'} is selected from the group consisting of methyl, ethyl, and trifluoromethyl; or

R^{1'} and R^{2'} are joined to form a spirocyclic ring containing 3 to 7 carbon atoms;

and

R^{3'} is selected from the group consisting of C₁ to C₄ alkyl; or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug of formula I or formula II.

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2(Currently Amended). The method according to claim 1, wherein said compound of ~~formula I or~~ formula II and said selective estrogen receptor modulator are delivered in a single composition.

3(Currently Amended). The method according to claim 1, wherein said compound of ~~formula I or~~ formula II and said selective estrogen receptor modulator are delivered separately.

4(Original). The method according to claim 1, wherein said selective estrogen receptor modulator is selected from the group consisting of EM-800, EM-652, raloxifene hydrochloride, arzoxifene, lasofoxifene, droloxifene, idoxifene, levomeloxifene, centchroman, nafoxidene, tamoxifen citrate, 4-hydroxytamoxifen citrate, clomiphene citrate, toremifene citrate, pipendoxifene, and bazedoxifene.

5(Original). The method according to claim 1, wherein said compound is delivered at a daily dosage of about 0.1 to about 50 mg.

6(Original). The method according to claim 1, wherein said regimen comprises delivering said composition daily for 1 to about 21 days, wherein said regimen is a cycle which is repeated monthly.

7(Currently Amended). ~~Then~~ The method according to claim 1, wherein said selective estrogen receptor modulator is delivered at a daily dosage of about 0.2 to about 100 mg.

8-24(Canceled).

25(Currently Amended). The method according to claim 1 wherein said compound of ~~formula I~~ is selected from the group consisting of 6-(3-Chlorophenyl)-4,4-

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dimethyl 1,4 dihydro benzo[d][1,3]oxazin-2-thione, 4 (4,4 Dimethyl 2-thioxo 1,4 dihydro 2H benzo[d][1,3]oxazin-6-yl) thiophene 2-carbonitrile, 3 (4,4 Dimethyl 2-thioxo 1,4 dihydro 2H benzo[d][1,3]oxazin-6-yl) 5-fluorobenzonitrile, 3 (4,4 Dimethyl 2-thioxo 1,4 dihydro 2H benzo[d][1,3]oxazin-6-yl) benzonitrile, 6 (3-fluorophenyl) 4-methyl 1,4 dihydro 2H-3,1-benzoxazine 2-thione, 5 (4,4 Dimethyl 2-thioxo 1,4 dihydro 2H-3,1-benzoxazine 6-yl) 4-methylthiophene 2-carbonitrile, tert-Butyl 2-cyano-5 (4,4 dimethyl 2-thioxo 1,4 dihydro 2H-3,1-benzoxazine 6-yl) 1H-pyrrole-1-carboxylate, 5 (4,4 Dimethyl 2-thioxo 1,4 dihydro 2H-3,1-benzoxazine 6-yl) 1H-pyrrole-2-carbonitrile, [6 (4,4 dimethyl 2-thioxo 1,4 dihydro 2H-3,1-benzoxazine 6-yl) pyridin-2-yl]acetonitrile, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, 5 (4,4 dimethyl 2-thioxo 1,4 dihydro 2H-3,1-benzoxazin-6-yl) 1H-pyrrole 2-carbethiamide, 5 (4,4 Dimethyl 2-thioxo 1,4 dihydro 2H benzo[d][1,3]oxazin-6-yl) thiophene 3-carbonitrile, and 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-ethyl-1H-pyrrole-2-carbonitrile, 4 (1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazin-4,1-cyclohexan]-6-yl) 2-thiophene-carbonitrile, 5 (4,4-Dimethyl 2-thioxo 1,4 dihydro 2H-3,1-benzoxazine 6-yl) 2-fluorobenzonitrile, 6 (5-Bromo-3-yl) 4,4 dimethyl 1,4 dihydro 2H-3,1-benzoxazine 2-thione, 6 (3-Chloro-5-fluorophenyl) 4,4 dimethyl 1,4 dihydro 2H-3,1-benzoxazine 2-thione, 6 (3-Bromo-5-methylphenyl) 4,4 dimethyl 1,4 dihydro 2H-3,1-benzoxazine 2-thione, 6 (3-Bromo-5-trifluoromethoxyphenyl) 4,4 dimethyl 1,4 dihydro 2H-3,1-benzoxazine 2-thione, 3 (1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazin-4,1-cyclohexan]-6-yl) 5-fluorobenzonitrile, 3 (4,4-Dimethyl 2-thioxo 1,4 dihydro 2H-3,1-benzoxazin-6-yl) 5-methylbenzonitrile, 6 (3,5-Dichlorophenyl) 4,4 dimethyl 1,4 dihydro 2H-3,1-benzoxazine 2-thione, 5 (4,4-Dimethyl 1,2-thioxo 1,4 dihydro 2H-3,1-benzoxazin-6-yl) isophthalonitrile, 5 (4,4 Dimethyl 2-thioxo 1,4 dihydro 2H-3,1-benzoxazin-6-yl) 2-furanonitrile, 4,4 Diethyl 6-(3-nitrophenyl) 1,4 dihydro 2H-3,1-benzoxazine 2-thione, 6-(3-Chlorophenyl) 4-methyl 4-phenyl 1,4 dihydro 2H-3,1-benzoxazine 2-thione, 4-Allyl-6-(3-chlorophenyl) 4-methyl 1,4 dihydro 2H-3,1-benzoxazine 2-thione, 3-Chloro-5-(4,4-dimethyl 2-thioxo 1,4 dihydro 2H-3,1-benzoxazin-6-yl)benzonitrile, 6 (3,5-

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~~Difluorophenyl) 4,4 dimethyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 6 (3 Fluoro 5 methoxyphenyl) 4,4 dimethyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 3 (4,4 Dimethyl 2 thioxe 1,4 dihydro 2H 3,1 benzoxazin 6 yl) 5 methoxybenzonitrile, 6 (3 Fluorophenyl) 4,4 dimethyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 6 [3 Fluoro 5 (trifluoromethyl)phenyl] 4,4 dimethyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 6 (2 Fluorophenyl) 4,4 dimethyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 6 (3,4 Difluorophenyl) 4,4 dimethyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 6 (4 Fluorophenyl) 4,4 dimethyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 3 (4,4 Dimethyl 2 thioxe 1,4 dihydro 2H 3,1 benzoxazin 6 yl) 4 fluorobenzonitrile, 6 (2,3 Difluorophenyl) 4,4 dimethyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 3 (8 Bromo 4,4 dimethyl 2 thioxe 1,4 dihydro 2H 3,1 benzoxazin 6 yl) 5 fluorobenzonitrile, 4,4 Dimethyl 6 (3 nitrophenyl) 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 6 (3 Chlorophenyl) 4,4 diethyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 6 (3 Methoxyphenyl) 4,4 dimethyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 6 (2 Chlorophenyl) 4,4 dimethyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 4 Benzyl 6 (3 chlorophenyl) 4 methyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 6 (3 Bromo 5 fluorophenyl) 4,4 dimethyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 5 (4,4 Dimethyl 2 thioxe 1,4 dihydro 2H 3,1 benzoxazin 6 yl) thiophene 2 carbonitrile, 3 Fluoro 5 (8 fluoro 4,4 dimethyl 2 thioxe 1,4 dihydro 2H 3,1 benzoxazin 6 yl) benzonitrile, 3 (1,2 Dihydro 2 thioxospiro[4H-3,1 benzoxazine 4,1 cyclohexan] 6 yl) benzonitrile, 5 (1,2 Dihydro 2 thioxospiro[4H 3,1 benzoxazine 4,1 cyclohexan] 6 yl) 4 methyl 2 thiophenecarbonitrile, 5 (1,2 Dihydro 2 thioxospiro[4H 3,1 benzoxazine 4,1 cyclohexan] 6 yl) 2 thiophenecarbonitrile, 6 (3 Chloro 4 fluorophenyl) 4,4 dimethyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, 5 (4,4 Dimethyl 2 thioxe 1,4 dihydro 2H 3,1 benzoxazin 6 yl) 4 propylthiophene 2 carbonitrile, 4 (4,4 Dimethyl 2 thioxe 1,4 dihydro 2H 3,1 benzoxazin 6 yl) 2 furonitrile, 4 Butyl 5 (4,4 dimethyl 2 thioxe 1,4 dihydro 2H 3,1 benzoxazin 6 yl) thiophene 2 carbonitrile, 6 (3 Bromophenyl) 4,4 dimethyl 1,4 dihydro 2H 3,1 benzoxazine 2 thione, and 2 (4,4 Dimethyl 2 thioxe 1,4~~

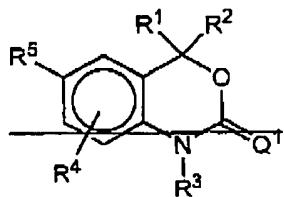
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~~dihydro 2H-3,1-benzoxazin-6-yl)thiophene-3-carbonitrile, or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.~~

26(Canceled).

27(Currently Amended). The method according to claim 414, wherein said compound of formula II is selected from the group consisting of: 5-(4-ethyl-4-methyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, 5-(4,4-diethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, 1-methyl-5-(2-thioxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclobutan]-6-yl)-1H-pyrrole-2-carbonitrile, 1-methyl-5-(2-thioxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclohexan]-6-yl)-1H-pyrrole-2-carbonitrile, 1-methyl-5-(2-thioxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclopentan]-6-yl)-1H-pyrrole-2-carbonitrile, 1-methyl-5-[2-thioxo-4,4-bis(trifluoromethyl)-1,4-dihydro-2H-3,1-benzoxazine-6-yl]-1H-pyrrole-2-carbonitrile, and prodrugs, metabolites, and pharmaceutically acceptable salts thereof.

28(Currently Amended). A pharmaceutical kit useful for inducing contraception, said kit comprising a compound of ~~formula I or formula II~~ and at least one selective estrogen receptor modulator, wherein ~~formula I~~ is:



+

wherein:

~~R¹ and R² are independent substituents selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₂ to C₆ alkenyl, C₃ to C₆ cycloalkyl, phenyl, and thiophene;~~

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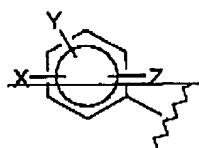
or R^1 and R^2 are fused to form a carbon-based 3 to 8 membered saturated spirocyclic ring;

R^3 is H;

R^4 is H;

R^5 is selected from the group consisting of (i) and (ii):

(i) a substituted benzene ring having the structure:



X is selected from the group consisting of halogen, CN, C_1 to C_4 alkyl, substituted C_1 to C_4 alkyl, C_1 to C_4 alkoxy, NO_2 , and C_1 to C_4 perfluoroalkyl;

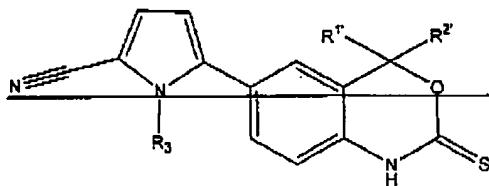
Y and Z are independent substituents selected from the group consisting of H, halogen, CN, NO_2 , C_1 to C_4 alkoxy, C_1 to C_4 alkyl, and substituted C_1 to C_4 alkyl; and

(ii) a five or six membered carbon-based heterocyclic ring having in its backbone 1 heteroatom selected from the group consisting of O, S, and NR^6 and having one or two independent substituents selected from the group consisting of H, halogen, CN, C_1 to C_4 alkyl, and substituted C_1 to C_4 alkyl;

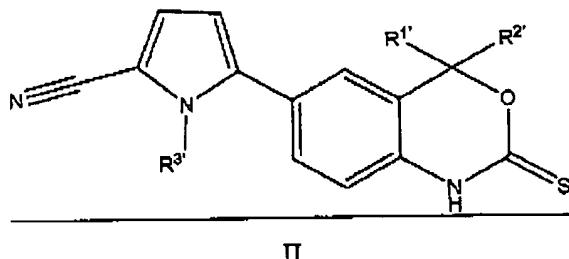
R^6 is selected from the group consisting of H, C_1 to C_4 alkyl, and C_1 to C_4 CO_2 alkyl;

Q^1 is S;

and formula II is:



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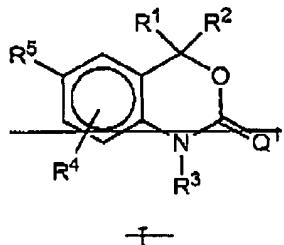
wherein:

 $R^{1'}$ is selected from the group consisting of methyl, ethyl, and trifluoromethyl; $R^{2'}$ is selected from the group consisting of methyl, ethyl, and trifluoromethyl; or $R^{1'}$ and $R^{2'}$ are joined to form a spirocyclic ring containing 3 to 7 carbon atoms;

and

 $R^{3'}$ is C_1 to C_4 alkyl;and or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.

29(Currently Amended). A contraceptive regimen comprising the periodic and discontinuous delivery of a compound of formula I or formula II, or a tautomer thereof, and a pharmaceutically effective amount of one or more of a selective estrogen receptor modulator to a female of child-bearing age, wherein formula I is:



wherein:

R^1 and R^2 are independent substituents selected from the group consisting of H, C_1 to C_6 alkyl, substituted C_1 to C_6 alkyl, C_2 to C_6 alkenyl, substituted C_2 to C_6 alkenyl, C_3 to C_6 alkynyl, substituted C_2 to C_6 alkynyl, C_3 to C_8 cycloalkyl, substituted C_3 to C_8 cycloalkyl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR^A , and $NR^B COR^A$;

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or R^1 and R^2 are fused to form a ring selected from the group consisting of a), b) and c), wherein said ring is optionally substituted by from 1 to 3 substituents selected from the group consisting of H and C₁ to C₃ alkyl;

- a) — a carbon-based 3 to 8 membered saturated spirocyclic ring;
- b) — a carbon-based 3 to 8 membered spirocyclic ring having one or more carbon-carbon double bonds; and
- c) — a 3 to 8 membered spirocyclic ring having in its backbone one to three heteroatoms selected from the group consisting of O, S and N;

— R^A is selected from the group consisting of H, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, aryl, substituted aryl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, amino, C₁ to C₃ aminealkyl, and substituted C₁ to C₃ aminealkyl;

— R^B is selected from the group consisting of H, C₁ to C₃ alkyl, and substituted C₁ to C₃ alkyl;

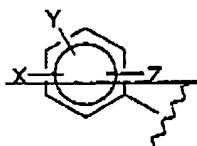
— R^3 is selected from the group consisting of H, OH, NH₂, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₂ to C₆ alkenyl, substituted C₂ to C₆ alkenyl, alkynyl, substituted alkynyl, and COR^C;

— R^6 is selected from the group consisting of H, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, aryl, substituted aryl, C₁ to C₄ alkoxy, substituted C₁ to C₄ alkoxy, C₁ to C₄ aminealkyl, and substituted C₁ to C₄ aminealkyl;

— R^4 is selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₁ to C₆ alkoxy, substituted C₁ to C₆ alkoxy, C₁ to C₆ aminealkyl, and substituted C₁ to C₆ aminealkyl;

— R^5 is selected from the group consisting of (i) and (ii):

- (i) — a substituted benzene ring having the structure:



X is selected from the group consisting of halogen, CN, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃

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thioalkyl, substituted C₁ to C₃ thioalkyl, C₁ to C₃ aminoalkyl, substituted C₁ to C₃ aminoalkyl, NO₂, C₁ to C₃ perfluoroalkyl, substituted C₁ to C₃ perfluoroalkyl, 5 or 6 membered carbon based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR^D, OCOR^D, and NR^ECOR^D;

R^D is selected from the group consisting of H, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, aryl, substituted aryl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ aminoalkyl, and substituted C₁ to C₃ aminoalkyl;

R^E is selected from the group consisting of H, C₁ to C₃ alkyl, and substituted C₁ to C₃ alkyl;

Y and Z are independent substituents selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, C₁ to C₃ thioalkyl, and substituted C₁ to C₃ thioalkyl; and

(ii) a five or six membered carbon based heterocyclic ring having in its backbone 1, 2, or 3 heteroatoms selected from the group consisting of O, S, SO, SO₂, and NR^E and having one or two independent substituents selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ aminoalkyl, substituted C₁ to C₃ aminoalkyl, C₁ to C₃ perfluoroalkyl, substituted C₁ to C₃ perfluoroalkyl, 5 or 6 membered carbon based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon based heterocyclic ring having in its backbone 1 to 3 heteroatoms, C₁ to C₃ thioalkyl, substituted C₁ to C₃ thioalkyl, COR^F, and NR^GCOR^F;

R^F is selected from the group consisting of H, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, aryl, substituted aryl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ aminoalkyl, and substituted C₁ to C₃ aminoalkyl;

R^G is selected from the group consisting of H, C₁ to C₃ alkyl, and substituted C₁ to C₃ alkyl;

R^H is selected from the group consisting of H, C₁ to C₃ alkyl, and C₁ to C₄ CO₂alkyl;

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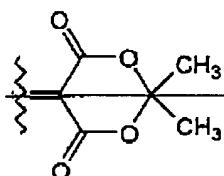
Q^+ is selected from the group consisting of S , NR^7 , and CR^8R^9 ;

R^7 is selected from the group consisting of CN , C_1 to C_6 alkyl, substituted C_1 to C_6 alkyl, C_2 to C_8 cycloalkyl, substituted C_2 to C_8 cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, SO_2CF_3 , OR^{14} , and $NP^{11+}R^{12}$;

R^8 and R^9 are independent substituents selected from the group consisting of H , C_1 to C_6 alkyl, substituted C_1 to C_6 alkyl, C_2 to C_8 cycloalkyl, substituted C_2 to C_8 cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, NO_2 , CN , and CO_2R^{10} ;

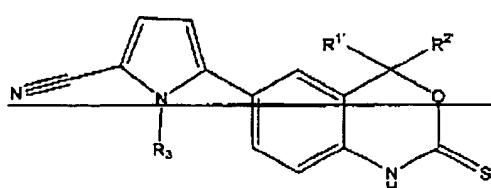
R^{10} is selected from the group consisting of C_1 to C_2 alkyl and substituted C_1 to C_3 alkyl;

or CR^8R^9 comprise a six-membered ring having the structure:

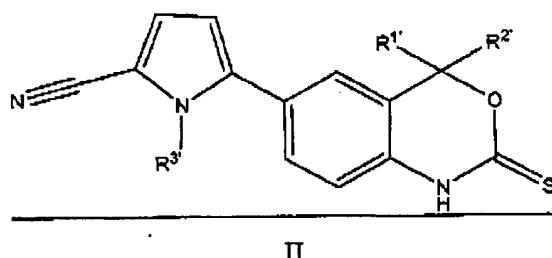


R^{11} and R^{12} are independently selected from the group consisting of H , C_1 to C_6 alkyl, substituted C_1 to C_6 alkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, acyl, substituted acyl, sulfonyl, and substituted sulfonyl;

and formula II is:



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wherein:

$R^{1'}$ is selected from the group consisting of methyl, ethyl, and trifluoromethyl;

$R^{2'}$ is selected from the group consisting of methyl, ethyl, and trifluoromethyl; or

$R^{1'}$ and $R^{2'}$ are joined to form a spirocyclic ring containing 3 to 7 carbon atoms;

and

$R^{3'}$ is selected from the group consisting of C_1 to C_4 alkyl;

or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug of formula I or formula II.

30(Currently Amended). The regimen according to claim 29, comprising delivering said compound of formula I or formula II and said selective estrogen receptor modulator separately.

31(Currently Amended). The regimen according to claim 29, comprising delivering said compound of formula I or formula II and said selective estrogen receptor modulator in a single composition.

32(Previously Presented). The regimen according to claim 29, further comprising delivering a placebo.

33(Previously Presented). The regimen according to claim 29 which comprises 28 days.

AHPWA25AUSA

34(Currently Amended). The regimen according to claim 33, wherein said regimen comprises delivering said compound of formula I or formula II and said selective estrogen receptor modulator for 14 to 24 days.

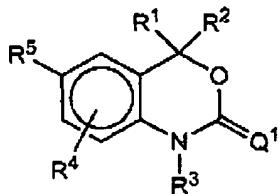
35(Currently Amended). The regimen according to claim 33, wherein said regimen comprises:

- (a) delivering said compound of formula I or formula II and said selective estrogen receptor modulator for the first 14 to 24 days of said 28 day regimen; and
- (b) delivering said selective estrogen receptor modulator alone for 1 to 11 days beginning on any day between days 14 and 24.

36(Currently Amended). The regimen according to claim 35, wherein said regimen further comprises:

- (c) delivering a placebo for 1 to 10 days during the period of time where said compound of formula II and said selective estrogen receptor modulator are not delivered.

37(Currently Amended). The A contraceptive regimen comprising the periodic and discontinuous delivery of a compound of formula I or II and a pharmaceutically effective amount of one or more of a selective estrogen receptor modulator to a female of child-bearing age, wherein formula I is: according to claim 33



I

wherein:

R¹ and R² are independent substituents selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₂ to C₆ alkenyl, substituted C₂ to C₆ alkenyl, C₂ to C₆ alkynyl, substituted C₂ to C₆ alkynyl, C₃ to C₈ cycloalkyl, substituted C₃ to C₈

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cycloalkyl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR^{A} , and $\text{NR}^{\text{B}}\text{COR}^{\text{A}}$:

or R^1 and R^2 are fused to form a ring selected from the group consisting of a), b) and c), wherein said ring is optionally substituted by from 1 to 3 substituents selected from the group consisting of H and C_1 to C_3 alkyl;

a) a carbon-based 3 to 8 membered saturated spirocyclic ring;
b) a carbon-based 3 to 8 membered spirocyclic ring having one or more carbon-carbon double bonds; and

c) a 3 to 8 membered spirocyclic ring having in its backbone one to three heteroatoms selected from the group consisting of O, S and N;

R^{A} is selected from the group consisting of H, C_1 to C_3 alkyl, substituted C_1 to C_3 alkyl, aryl, substituted aryl, C_1 to C_3 alkoxy, substituted C_1 to C_3 alkoxy, amino, C_1 to C_3 aminoalkyl, and substituted C_1 to C_3 aminoalkyl;

R^{B} is selected from the group consisting of H, C_1 to C_3 alkyl, and substituted C_1 to C_3 alkyl;

R^{3} is selected from the group consisting of H, OH, NH_2 , C_1 to C_6 alkyl, substituted C_1 to C_6 alkyl, C_3 to C_6 alkynyl, substituted C_3 to C_6 alkynyl, alkynyl, substituted alkynyl, and COR^{C} ;

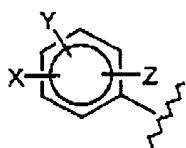
R^{C} is selected from the group consisting of H, C_1 to C_4 alkyl, substituted C_1 to C_4 alkyl, aryl, substituted aryl, C_1 to C_4 alkoxy, substituted C_1 to C_4 alkoxy, C_1 to C_4 aminoalkyl, and substituted C_1 to C_4 aminoalkyl;

R^{4} is selected from the group consisting of H, halogen, CN, NO_2 , C_1 to C_6 alkyl, substituted C_1 to C_6 alkyl, C_1 to C_6 alkoxy, substituted C_1 to C_6 alkoxy, C_1 to C_6 aminoalkyl, and substituted C_1 to C_6 aminoalkyl;

R^{5} is selected from the group consisting of (i) and (ii):

(i) a substituted benzene ring having the structure:

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X is selected from the group consisting of halogen, CN, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ thioalkyl, substituted C₁ to C₃ thioalkyl, C₁ to C₃ aminoalkyl, substituted C₁ to C₃ aminoalkyl, NO₂, C₁ to C₃ perfluoroalkyl, substituted C₁ to C₃ perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR^D, OCOR^D, and NR^ECOR^D:

R^D is selected from the group consisting of H, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, aryl, substituted aryl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ aminoalkyl, and substituted C₁ to C₃ aminoalkyl;

R^E is selected from the group consisting of H, C₁ to C₃ alkyl, and substituted C₁ to C₃ alkyl;

Y and Z are independent substituents selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, C₁ to C₃ thioalkyl, and substituted C₁ to C₃ thioalkyl; and

(ii) a five or six membered carbon-based heterocyclic ring having in its backbone 1, 2, or 3 heteroatoms selected from the group consisting of O, S, SO, SO₂, and NR^G and having one or two independent substituents selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ aminoalkyl, substituted C₁ to C₃ aminoalkyl, C₁ to C₃ perfluoroalkyl, substituted C₁ to C₃ perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, C₁ to C₃ thioalkyl, substituted C₁ to C₃ thioalkyl, COR^F, and NR^GCOR^F;

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R^F is selected from the group consisting of H, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, aryl, substituted aryl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ aminoalkyl, and substituted C₁ to C₃ aminoalkyl;

R^G is selected from the group consisting of H, C₁ to C₃ alkyl, and substituted C₁ to C₃ alkyl;

R^6 is selected from the group consisting of H, C₁ to C₃ alkyl, and C₁ to C₄ CO₂alkyl;

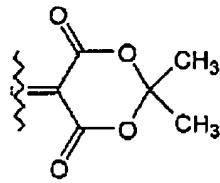
Q^1 is selected from the group consisting of S, NR⁷, and CR⁸R⁹;

R^7 is selected from the group consisting of CN, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₁ to C₈ cycloalkyl, substituted C₃ to C₈ cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, SO₂CF₃, OR¹¹, and NR¹¹R¹²;

R^8 and R^9 are independent substituents selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₁ to C₈ cycloalkyl, substituted C₃ to C₈ cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, NO₂, CN, and CO₂R¹⁰;

R^{10} is selected from the group consisting of C₁ to C₃ alkyl and substituted C₁ to C₃ alkyl;

or CR⁸R⁹ comprise a six membered ring having the structure:

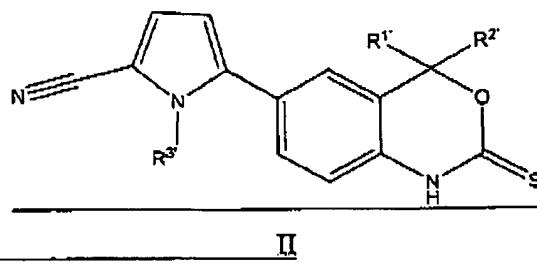


R^{11} and R^{12} are independently selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring

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having in its backbone 1 to 3 heteroatoms, acyl, substituted acyl, sulfonyl, and substituted sulfonyl;

and formula II is:



wherein:

R¹ is selected from the group consisting of methyl, ethyl, and trifluoromethyl;

R² is selected from the group consisting of methyl, ethyl, and trifluoromethyl; or

R¹ and R² are joined to form a spirocyclic ring containing 3 to 7 carbon atoms;

and

R³ is C₁ to C₄ alkyl;

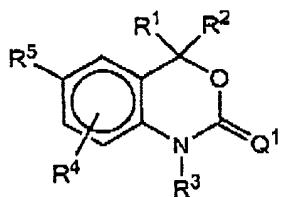
or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug of formula I or formula II, wherein said regimen comprises:

(a) delivering said compound of formula I or formula II for the first 18 to 21 days of a 28 day regimen; and

(b) delivering said selective estrogen receptor modulator alone for 1 to 7 days following delivery of (a).

38(Currently Amended). The A contraceptive regimen comprising the periodic and discontinuous delivery of a compound of formula I or II and a pharmaceutically effective amount of one or more of a selective estrogen receptor modulator to a female of child-bearing age, wherein formula I is: according to claim 33

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I

wherein:

R¹ and R² are independent substituents selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₂ to C₆ alkenyl, substituted C₂ to C₆ alkenyl, C₂ to C₆ alkynyl, substituted C₂ to C₆ alkynyl, C₃ to C₈ cycloalkyl, substituted C₃ to C₈ cycloalkyl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR^A, and NR^BCOR^A,

or R¹ and R² are fused to form a ring selected from the group consisting of a), b) and c), wherein said ring is optionally substituted by from 1 to 3 substituents selected from the group consisting of H and C₁ to C₃ alkyl;

- a) a carbon-based 3 to 8 membered saturated spirocyclic ring;
- b) a carbon-based 3 to 8 membered spirocyclic ring having one or more carbon-carbon double bonds; and
- c) a 3 to 8 membered spirocyclic ring having in its backbone one to three heteroatoms selected from the group consisting of O, S and N;

R^A is selected from the group consisting of H, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, aryl, substituted aryl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, amino, C₁ to C₃ aminoalkyl, and substituted C₁ to C₃ aminoalkyl;

R^B is selected from the group consisting of H, C₁ to C₃ alkyl, and substituted C₁ to C₃ alkyl;

R³ is selected from the group consisting of H, OH, NH₂, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₂ to C₆ alkenyl, substituted C₂ to C₆ alkenyl, alkynyl, substituted alkynyl, and COR^C;

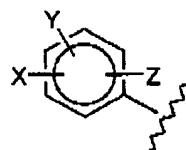
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R^C is selected from the group consisting of H, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, aryl, substituted aryl, C₁ to C₄ alkoxy, substituted C₁ to C₄ alkoxy, C₁ to C₄ aminoalkyl, and substituted C₁ to C₄ aminoalkyl;

R⁴ is selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₁ to C₆ alkoxy, substituted C₁ to C₆ alkoxy, C₁ to C₆ aminoalkyl, and substituted C₁ to C₆ aminoalkyl;

R⁵ is selected from the group consisting of (i) and (ii):

(i) a substituted benzene ring having the structure:



X is selected from the group consisting of halogen, CN, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ thioalkyl, substituted C₁ to C₃ thioalkyl, C₁ to C₃ aminoalkyl, substituted C₁ to C₃ aminoalkyl, NO₂, C₁ to C₃ perfluoroalkyl, substituted C₁ to C₃ perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR^D, OCOR^D, and NR^ECOR^D;

R^D is selected from the group consisting of H, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, aryl, substituted aryl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ aminoalkyl, and substituted C₁ to C₃ aminoalkyl;

R^E is selected from the group consisting of H, C₁ to C₃ alkyl, and substituted C₁ to C₃ alkyl;

Y and Z are independent substituents selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, C₁ to C₃ thioalkyl, and substituted C₁ to C₃ thioalkyl; and

(ii) a five or six membered carbon-based heterocyclic ring having in its backbone 1, 2, or 3 heteroatoms selected from the group consisting of O, S, SO, SO₂, and NR⁶ and having one or two independent substituents selected from the group consisting

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of H, halogen, CN, NO₂, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ aminoalkyl, substituted C₁ to C₃ aminoalkyl, C₁ to C₃ perfluoroalkyl, substituted C₁ to C₃ perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, C₁ to C₃ thioalkyl, substituted C₁ to C₃ thioalkyl, COR^F, and NR^GCOR^F.

R^F is selected from the group consisting of H, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, aryl, substituted aryl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ aminoalkyl, and substituted C₁ to C₃ aminoalkyl;

R^G is selected from the group consisting of H, C₁ to C₃ alkyl, and substituted C₁ to C₃ alkyl;

R⁶ is selected from the group consisting of H, C₁ to C₃ alkyl, and C₁ to C₄ CO₂alkyl;

Q¹ is selected from the group consisting of S, NR⁷, and CR⁸R⁹;

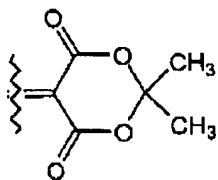
R⁷ is selected from the group consisting of CN, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₃ to C₈ cycloalkyl, substituted C₃ to C₈ cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, SO₂CF₃, OR¹¹, and NR¹¹R¹²;

R⁸ and R⁹ are independent substituents selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₁ to C₈ cycloalkyl, substituted C₃ to C₈ cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, NO₂, CN, and CO₂R¹⁰;

R¹⁰ is selected from the group consisting of C₁ to C₃ alkyl and substituted C₁ to C₃ alkyl;

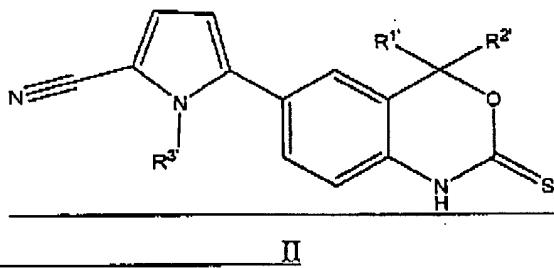
or CR⁸R⁹ comprise a six membered ring having the structure:

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R¹¹ and R¹² are independently selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, acyl, substituted acyl, sulfonyl, and substituted sulfonyl;

and formula II is:



wherein:

R^{1'} is selected from the group consisting of methyl, ethyl, and trifluoromethyl;

R^{2'} is selected from the group consisting of methyl, ethyl, and trifluoromethyl; or

R^{1'} and R^{2'} are joined to form a spirocyclic ring containing 3 to 7 carbon atoms;

and

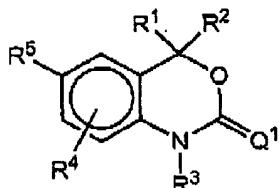
R^{3'} is C₁ to C₄ alkyl;

or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug of formula I or formula II, wherein said regimen comprises:

- (a) delivering said compound of formula I or formula II and an estrogen for the first 21 days of a 28 day regimen; and
- (b) delivering said selective estrogen receptor modulator alone from days 22 to 24 of said 28 day regimen for 1 to 4 days.

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39(Currently Amended). The method A contraceptive regimen comprising the periodic and discontinuous delivery of a compound of formula I or II and a pharmaceutically effective amount of one or more of a selective estrogen receptor modulator to a female of child-bearing age, wherein formula I is: according to claim 29



I

wherein:

R¹ and R² are independent substituents selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₂ to C₆ alkenyl, substituted C₂ to C₆ alkenyl, C₂ to C₆ alkynyl, substituted C₂ to C₆ alkynyl, C₁ to C₈ cycloalkyl, substituted C₁ to C₈ cycloalkyl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR^A, and NR^BCOR^A;

or R¹ and R² are fused to form a ring selected from the group consisting of a), b) and c), wherein said ring is optionally substituted by from 1 to 3 substituents selected from the group consisting of H and C₁ to C₃ alkyl;

- a) a carbon-based 3 to 8 membered saturated spirocyclic ring;
- b) a carbon-based 3 to 8 membered spirocyclic ring having one or more carbon-carbon double bonds; and
- c) a 3 to 8 membered spirocyclic ring having in its backbone one to three heteroatoms selected from the group consisting of O, S and N;

R^A is selected from the group consisting of H, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, aryl, substituted aryl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, amino, C₁ to C₃ aminoalkyl, and substituted C₁ to C₃ aminoalkyl;

R^B is selected from the group consisting of H, C₁ to C₃ alkyl, and substituted C₁ to C₃ alkyl;

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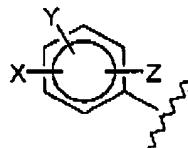
R³ is selected from the group consisting of H, OH, NH₂, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₃ to C₆ alkenyl, substituted C₃ to C₆ alkenyl, alkynyl, substituted alkynyl, and COR^C:

R^C is selected from the group consisting of H, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, aryl, substituted aryl, C₁ to C₄ alkoxy, substituted C₁ to C₄ alkoxy, C₁ to C₄ aminoalkyl, and substituted C₁ to C₄ aminoalkyl;

R⁴ is selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₁ to C₆ alkoxy, substituted C₁ to C₆ alkoxy, C₁ to C₆ aminoalkyl, and substituted C₁ to C₆ aminoalkyl;

R⁵ is selected from the group consisting of (i) and (ii):

(i) a substituted benzene ring having the structure:



X is selected from the group consisting of halogen, CN, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ thioalkyl, substituted C₁ to C₃ thioalkyl, C₁ to C₃ aminoalkyl, substituted C₁ to C₃ aminoalkyl, NO₂, C₁ to C₃ perfluoroalkyl, substituted C₁ to C₃ perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR^D, OCOR^D, and NR^ECOR^D:

R^D is selected from the group consisting of H, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, aryl, substituted aryl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ aminoalkyl, and substituted C₁ to C₃ aminoalkyl;

R^E is selected from the group consisting of H, C₁ to C₃ alkyl, and substituted C₁ to C₃ alkyl;

Y and Z are independent substituents selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, C₁ to C₃ thioalkyl, and substituted C₁ to C₃ thioalkyl; and

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(ii) a five or six membered carbon-based heterocyclic ring having in its backbone 1, 2, or 3 heteroatoms selected from the group consisting of O, S, SO, SO₂, and NR⁶ and having one or two independent substituents selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ aminoalkyl, substituted C₁ to C₃ aminoalkyl, C₁ to C₃ perfluoroalkyl, substituted C₁ to C₃ perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, C₁ to C₃ thioalkyl, substituted C₁ to C₃ thioalkyl, COR^F, and NR^GCOR^F:

R^F is selected from the group consisting of H, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, aryl, substituted aryl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ aminoalkyl, and substituted C₁ to C₃ aminoalkyl;

R^G is selected from the group consisting of H, C₁ to C₃ alkyl, and substituted C₁ to C₃ alkyl;

R⁶ is selected from the group consisting of H, C₁ to C₃ alkyl, and C₁ to C₄ CO₂alkyl;

Q¹ is selected from the group consisting of S, NR⁷, and CR⁸R⁹.

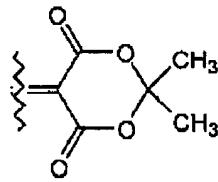
R⁷ is selected from the group consisting of CN, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₃ to C₈ cycloalkyl, substituted C₃ to C₈ cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, SO₂CF₃, OR¹¹, and NR¹¹R¹²;

R⁸ and R⁹ are independent substituents selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₃ to C₈ cycloalkyl, substituted C₃ to C₈ cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, NO₂, CN, and CO₂R¹⁰.

R¹⁰ is selected from the group consisting of C₁ to C₃ alkyl and substituted C₁ to C₃ alkyl;

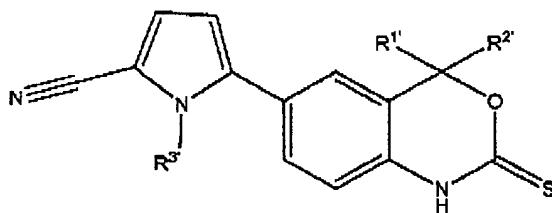
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or CR⁸R⁹ comprise a six membered ring having the structure:



R¹¹ and R¹² are independently selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, acyl, substituted acyl, sulfonyl, and substituted sulfonyl;

and formula II is:



II

wherein:

R^{1'} is selected from the group consisting of methyl, ethyl, and trifluoromethyl;

R^{2'} is selected from the group consisting of methyl, ethyl, and trifluoromethyl; or

R^{1'} and R^{2'} are joined to form a spirocyclic ring containing 3 to 7 carbon atoms;

and

R^{3'} is C₁ to C₄ alkyl;

or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug of formula I or formula II, wherein said regimen comprises 28 days and the steps of:

(a) a first phase of the compound of formula I or formula II and said selective estrogen receptor modulator to be administered on for the first days 14 to 24 days of said regimen;

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- (b) a second phase of said selective estrogen receptor modulator to be administered ~~on days for 1 to 11 days of said regimen beginning on any day between days 14 and 24~~; and
- (c) a third phase of an orally and pharmaceutically acceptable placebo for ~~days 1 to 10 days of said regimen or a third phase in which component phase (a) or (b) is not administered for days 1 to 10 days of said regimen~~.

40(Currently Amended). The ~~method~~ regimen according to claim 39, wherein:

- (a) said first phase comprises 14 days;
- (b) said second phase comprises 7 days; and
- (c) said third phase comprises 7 days.